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STUDIES ON THE MECHANISM OF ALUMINUM ANHIDROSIS*

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The mode of action of topically applied aluminum chloride has been discussed previously (1–5). Some investigators postulate the effect is at the sweat pore opening (5); others state that aluminum allows for greater eccrine duct reabsorption (3, 4). These experiments were performed to clarify the site of action.

METHOD

The following compounds were used:

1. Aluminum chloride (10 and 20%) in distilled water.

2. Scopolamine hydrobromide (1%), as a control in a special buffered solution, the composition of which follows (adjusted to pH 3):

Ethyl alcohol	5.0%
Cetyl polyoxyethylene ether (Brij 58)	1.0%
Hydroxyethylcellulose	0.3%
Water	93.7%

The test agent was applied to the forearm twice daily without occlusion for four days, the other forearm acting as a control. On the fifth day 0.1 ml of 1:1,000 methacholine (Mecholyl®) was injected intradermally in both forearms as a sweat stimulator; sweat rates were recorded for 15 minutes with a modified Bullard sudorometer (6). A new treated site and a new control site on each forearm was stripped 25 times with cellophane tape; the new baseline water loss was determined to compensate for transepidermal water loss. The injections were repeated at both sites and sweat responses again measured for a 15 minute period.

A third site on each forearm was stripped to the glistening layer (up to 45 strips). The new baseline water loss was again established, both sites were challenged with 1:1,000 methacholine and readings were taken for a 15 minute period.

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Twelve healthy young volunteers comprised the test panel: four males and two females in the aluminum chloride study and four females and two males in the scopolamine study.

RESULTS

Scopolamine

Table I shows the per cent of sweat inhibition for each scopolamine control subject before stripping, after 25 strips, and again after stripping to the glistening layer. The range of inhibition was from 60 to 100 per cent and an average of 81 per cent for all subjects. After 25 strips the per cent of sweat inhibition ranged from 72 to 100 per cent, with an average of 88 per cent; and after 45 strips from 66 to 97 per cent, with an average of 85 per cent. Thus, stripping to glistening fails to negate scopolamine anhidrosis. This was expected as scopolamine acts directly on the secretory portion of the gland and should not be affected by removing the stratum corneum.

Aluminum Chloride

Table I also shows the per cent of inhibition for each aluminum chloride site before stripping and after 25 to 45 strips, respectively. The before stripping control showed a sweat inhibition ranging from 55 to 100 per cent, with an average of 79 per cent. After 25 strips inhibition ranged from 28 to 80 per cent, with an average of 53 per cent, and after 45 strips the range was 28 to 84 per cent, with an average of 52 per cent. Thus, stripping fails to ablate aluminum-induced anhidrosis. This data and that from other similar experiments suggests a tendency to slight diminution of the aluminum anhidrotic effect with stripping. However, these differences did not achieve statistical significance. This indicates that aluminum site of action is below the stratum corneum.

Another testing procedure consisted of soaking gauze pads with 20 per cent aluminum chloride, placing it on the forearm of four healthy adults and occluding with Saran Wrap® for 18 hours. When this was removed one hour

TABLE I

Scopolamine (% inhibition*)				
Subject	Sex	Before stripping	25 strip	Glistening (45 strips)
1	F	60	72	86
2	F	100	100	66
3	M	70	91	86
4	F	80	93	83
5	F	84	78	97
6	M	90	91	93
Average		81	88	85

10% Aluminum chloride (% inhibition)				
Subject	Sex	Before stripping	25 strip	45 strip
1	M	68	80	28
2	M	100	55	ND†
3	M	84	55	38
4	F	89	48	84
5	F	55	28	67
Average		79	53	52

* % Inhibition = $100 - \frac{\text{sweat rate of treated forearm}}{\text{sweat rate of untreated forearm (control)}}$

† ND = not done.

TABLE II

20% Aluminum chloride with 18 hour occlusion (% inhibition)

Subject	Sex	Control	25 strip	45 strip
1	M	100	100	96
2	F	94	94	94
3	F	90	90	90
4	M	100	100	88
Average		96	96	92

was allowed for air drying before testing with 1:1,000 methacholine. This established marked anhidrosis for 3–4 days. Surprisingly, sweating did not fully return for 8–14 days.

This occlusive application established 90 to 100 per cent inhibition of sweating at the test site (Table II). After 25 strips, inhibition remained between 90 and 100 per cent, with an average of 96 per cent, and after 45 strips, the inhibition varied between 88 to 96 per cent, with an average of 92 per cent. Initial inhibition of sweating was effective and remained so after stripping the skin 25 to 45 times. The initial degree of anhidrosis was greater than without occlusion; stripping again failed to alter this anhidrosis.

We next examined the effect of saline, water, and dry gauze on anhidrosis as additional experimental controls. A further experiment con-

TABLE III

18 hour occlusion (relative humidity)

Vehicle	Subject	Sex	Control	Test site	% Inhibition
15% NaCl	1	F	12.0	7.5	38
	2	F	2.5	2.5	0
	3	F	8.0	5.5	32
	4	F	8.5	7.5	12
	5	F	10.5	4.0	63
	6	F	13.0	13.0	0
	7	M	24.0	24.0	0
Average			11.2	9.1	20.7
Normal saline	1	F	6.0	4.0	33
	2	F	12.5	12.5	0
	3	F	8.5	8.5	0
	4	F	17.5	11.0	41
	5	F	13.5	13.5	0
	6	M	35.5	35.5	0
	7	F	12.0	8.0	33
	8	F	17.5	15.0	15
	9	M	35.0	27.0	23
Average			17.5	15.0	16.1
Distilled water	1	F	10.5	8.0	24
	2	F	8.0	8.0	0
	3	F	5.0	5.0	0
	4	F	5.0	5.0	0
	5	F	21.0	21.0	0
	6	M	14.5	3.5	76
	7	F	12.0	10.5	13
	8	M	35.0	34.5	2
	9	F	17.5	17.0	3
Average			14.2	12.5	13.1
Dry gauze	1	F	12.5	11.5	8
	2	F	18.0	18.0	0
	3	F	12.0	12.0	0
	4	F	12.0	10.0	17.0
	5	M	35.0	32.0	9.0
	6	F	17.5	15.0	16.1
Average			17.8	16.4	8.4

sisted of 18 hour occlusion with Saran Wrap® utilizing the following materials:

1. 15% NaCl in distilled water—a hypertonic solution
2. Normal saline solution
3. Distilled water
4. Dry gauze

The control site (other forearm) and the occluded site were tested with 1:1,000 methacholine 30 minutes after removal of occlusion. The purpose of this was to determine if occlusion with the above produced sweat inhibition. Inhibition with occlusion was evident in all cases, as shown in Table III. This varied as follows (Table III):

1. 15% NaCl—from 0% to 63%, with an average of 20%
3. Normal saline—from 0% to 41%, with an average of 16.1%
3. Distilled water—from 0% to 76%, with an average of 13.1%
4. Dry gauze—from 0% to 17% with an average of 8.4%

These results suggest that the effect of occlusion must be considered in testing for sweat inhibition, as occlusion alone produces inhibition in some individuals. The individual variation in occlusion induced anhidrosis was striking and requires further study for explanation.

DISCUSSION

As expected, these experiments demonstrated both agents effective in inhibiting sweating (using 1:1,000 methacholine for sweat induction). Scopolamine hydrobromide (1%) was more effective with an average inhibition of 80 per cent, as compared to 67 per cent with aluminum chloride. Inibition intensity varied greatly with aluminum chloride and was more consistent with scopolamine.

Sweat inhibition remained intact after 25 to 45 strippings, with averages consistently higher for scopolamine. It appears that the mode or site of action of both drugs is below the stratum corneum since stripping does not appear to affect the activity of the drug. If a mechanical block occurred at the sweat pore opening, as has been suggested, then the 25 and 45 strips would have ablated the inhibition. Our results show that in no case was this seen.

Therefore, the site of action must be somewhere below the stripped site, i.e. the duct or on the gland itself. This quantitative data supports the observations of Papa and Kligman (3, 4) obtained with colorimetric methods. Our observation of anhidrosis occurring in some subjects with hypertonic saline solution contrasts with the observation of Sarkany *et al.* (7). Their method of quantitation was observation of the sweat pore in surface replicas; our method consisted of measuring water loss. The highly variable occlusion noted here might not be observed with the former method.

SUMMARY

1. Experimental anhidrosis was produced with topical administration of 10 and 20 per cent aluminum chloride with and without occlusion, and 1 per cent scopolamine hydrobromide. To determine if stratum corneum or sweat pore blocking was a significant factor in the resulting anhidrosis the sites were stripped with cellophane tape to glistening. Sweat rates were determined with a modified Bullard sudorometer after intradermal injection of methacholine, 1:1,000.

2. Stripping failed to ablate the experimental anhidrosis induced by either aluminum chloride or scopolamine, supporting the hypothesis of Papa and Kligman that the effect of both is below the stratum corneum.

3. Additional controls performed with occlusive applications of hypertonic saline, normal saline, and distilled water indicated that short term occlusion produces a variable anhidrosis in some subjects.

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